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(54) SPECTROPHOTOMETRIC EXAMINATION OF TISSUE OF SMALL DIMENSION

SPEKTROPHOTOMETRISCHE UNTERSUCHUNG VON GEWEBEPROBEN KLEINER ABMESSUNGEN

EXAMEN SPECTROPHOTOMETRIQUE DE TISSUS DE FAIBLES DIMENSIONS

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Description

[0001] Continuous wave (CW) spectrophotometers have been widely used to determine *in vivo* concentration of an optically absorbing pigment (e.g., hemoglobin, oxyhemoglobin) in biological tissue. The CW spectrophotometers, for example, in pulse oximetry introduce light into a finger or the ear lobe to measure the light attenuation and then evaluate the concentration based on the Beer Lambert equation or modified Beer Lambert absorbance equation. The Beer Lambert equation (1) describes the relationship between the concentration of an absorbent constituent (C), the extinction coefficient (ε), the photon migration pathlength <L>, and the attenuated light intensity (I/I_0).

$$\frac{\log [I/I_0]}{<L>} = \Sigma \in_i C_i \qquad (1)$$

However, direct application of the Beer Lambert equation poses several problems. Since the tissue structure and physiology vary significantly, the optical pathlength of migrating photons also varies significantly and can not be simply determined from geometrical position of a source and detector. In addition, the photon migration pathlength itself is a function of the relative concentration of absorbing constituents. As a result, the pathlength through an organ with high blood hemoglobin concentration, for example, will be different from the same with a low blood hemoglobin concentration. Furthermore, the pathlength is frequently dependent upon the wavelength of the light since the absorption coefficient of many tissue constituents is wavelength dependent. One solution to this problem is to determine ε, C, and <L> at the same time, but this is not possible with the CW oximeters.

[0002] Furthermore, for quantitative measurement of tissue of a small volume (e.g., a finger) photon escape introduces a significant error since the photons escaped from the tissue are counted as absorbed.

[0003] There are several reasons for using in vivo tissue oximetry. Although the arterial oxygen saturation can be in vitro quantified, it is not possible to estimate the change in the hemoglobin oxygen concentration as it leaves an artery and enters the capillary bed. Neither is it possible to determine the intermediate value of oxygen saturation in a particular capillary bed from the venous drainage since no technique has been devised for drawing a blood sample directly from the capillary bed.

[0004] There are known time resolved (TRS-pulse) and phase modulation (PMS) spectrophotometers that can measure the average pathlength of migrating photons directly, but the proper quantitation of the time resolved or frequency resolved spectra can be performed only when the spectra are collected at a relatively large source-detector separation. This separation is difficult to achieve for a small volume of tissue such as the earlobe, a finger or a biopsy tissue.

[0005] EP-0204459 discloses an oximeter finger probe for use with an oximeter. The oximeter finger probe includes an upper housing and a lower housing pivotably hinged together at their distal ends such that a human finger can be inserted into the proximal end of the finger probe into a chamber formed therebetween. The finger probe contains at least one light emitter and at least one light detector situated within the upper and lower housings so as to allow light from the emitter to pass through the finger to the detector. At least one emitter is contained within an emitter housing that is pivotably mounted to the upper housing such that it conforms to the shape of the patient's finger when inserted into the chamber. The wiring for the emitter and the detector depends outwardly from the proximal end of the finger probe along the finger such that the wiring can be readily taped to the finger and, thus, help retain the finger probe in position on the finger. W0 92/20273 discloses different spectrophotometers including an oximeter for determining the oxygenation state of localized body tissue per se. The oximeter is constructed to be worn over a period of activity by a user and comprises a flexible, body-conformable support member which supports, adjacent the skin of a user, over the localized tissue of interest, at least a pair of spaced apart light sources, and intermediate thereof, a pair of wavelength-specific photo detectors. Each light source is exposed to transmit wavelengths of both the specific wavelengths toward the localized tissue of interest lying below the skin and below the associated subcutaneous fat layer of the user, and each detector is exposed to receive photons of the respective specific wavelength that have originated from each light source, and were scattered from the localized tissue and passed back to the detectors through the subcutaneous fat layer and skin of the user. The support member includes conformable barrier means disposed between each light source and the detectors. The barrier means is made of substance capable of conforming the contour of the wearer and preventing light energy proceeding laterally in the region of the barrier from reaching the detectors.

[0006] Therefore, there is a need for a spectrophotometric system and method for quantitative examination of a relatively small volume of biological tissue.

[0007] The preferred embodiment features a spectrophotometric system for examination of a relatively small volume of biological tissue of interest using visible or infra-red radiation.

[0008] According to one aspect of the invention, a spectrophotometric system for examination of a relatively small object of interest (e.g., biological tissue, organic or inorganic substance in a solid, liquid or gaseous state) uses visible or infra-red radiation introduced to a path passing through the object. The system includes a spectrophotometer with

an optical input port adapted to introduce radiation into the object and an optical detection port adapted to detect radiation that has migrated through a path in the object, photon escape preventing means arranged around the relatively small object of interest and adapted to limit escape of the introduced photons outside the object, and processing means adapted to determine an optical property of the object based on the changes between the introduced and the detected radiation.

[0009] According to another aspect of the invention, a system for examination of a relatively small volume of biological tissue of interest using visible or infra-red radiation includes a spectrophotometer with a light source adapted to introduce radiation at an optical input port, a detector adapted to detect radiation that has migrated through a path from the input port to an optical detection port, and a processor adapted to evaluate changes between the introduced and the detected radiation. The system also includes an optical medium of a relatively large volume, forming photon preventing means, having selectable scattering and absorptive properties, positioning means adapted to locate the biological tissue of interest into the migration path to create a tissue-medium optical path, the optical medium substantially limiting escape of photons from the tissue-medium optical path, and processing means adapted to determine a physiological property of the tissue based on the detected optical property of the tissue-medium optical path and the scattering or absorptive properties of the optical medium.

[0010] Preferred embodiments of these aspects of the invention include one or more of the following features.

[0011] The photon escape preventing means include an optical medium of a selectable optical property surrounding the object. The selectable optical property is an absorption or scattering coefficient.

[0012] The photon escape preventing means include an optical medium surrounding the object; the medium has at least one optical property substantially matched to the optical property of the object.

[0013] The spectrophotometer is a continuous wave spectrophotometer, a phase modulation spectroscopic unit or time resolved spectroscopic unit.

[0014] The determined physiological property is the hemoglobin saturation, the concentration of an enzyme or the concentration of a tissue substance such as glucose.

[0015] The system performs a single measurement or a continuous, time-dependent monitoring of the selected physiological property.

[0016] The above-described system operates by introducing into the object, surrounded by the photon escape preventing means, electromagnetic radiation of a selected wavelength and detecting radiation that has migrated in the object from the input port to the optical detection port. The system determines an optical property of the object based on the changes between the introduced and the detected radiation. In addition, different photon escape preventing means having a surrounding optical medium with the optical property comparable to the optical property of the object may be selected. Then, the system measures again the optical property of the object. The measurements may be repeated iteratively until the optical property of the surrounding medium is substantially matched to the optical property of the object.

[0017] Certain embodiments of the invention will now be described by way of example only and with reference to the accompanying drawings.

[0018] Fig. 1 is a diagrammatic view of a spectrophotometric system for examination of tissue of a relatively small dimension.

[0019] Figs. 2 and 2A show different views of a cylinder for preventing escape of photons during spectrophotometric measurements of a finger.

[0020] Fig. 2B shows a set of cylinders of preselected optical properties for a finger oximetry.

[0021] Fig. 3 is a diagrammatic view of an optical fiber holder for a spectrophotometric study of the head.

[0022] Fig. 4 is a diagrammatic view of a TRS test system used for finger examination.

[0023] Figs. 4A and 4B display measured values of the absorption coefficient measured in a test, and Fig. 4C displays their relative occurrence.

[0024] Figs. 4D and 4E display measured values of the scattering coefficient and their relative occurrence respectively.

[0025] Figs. 4F and 4G display calculated values of the hemoglobin saturation and their relative occurrence, respectively.

[0026] Referring to Fig. 1, a system 10 for examination of biological tissue of a relatively small volume, includes an optical medium 12 of selectable optical properties, a spectrophotometer 18, a titrimetric circulation system 30, and computer control 35. Biological tissue of interest 14, attached to a locator 15, is immersed in optical medium 12. Spectrophotometer 18 examines optical properties of medium 12 by employing visible or infra-red light conducted via light guides 20 and 22. Light guides 20 and 22, which in a preferred embodiment are optical fibers, are connected to a light source 24 and a light detector 23, respectively. Photons introduced at an optical input port 19 migrate in medium 12 through a scattering and absorptive path and are detected at a detection port 21. The selectable fixed geometry of input port 19 and detection port 21 controls the migration path, i.e., optical field 25.

[0027] System 30 is adapted to change precisely the scattering and absorptive properties of medium 12. Medium

12 includes intralipid solution (made by Kabi Vitrum, Inc., Clapton, NC) that exhibits scattering properties depending on its concentration and carbon black india ink that exhibits absorptive properties. The scattering or absorptive properties of medium 12 can be either maintained constant and uniform by properly mixing the solution or can be changed almost continuously by changing the concentration of the constituents in titration system 30. Tubes 32 and 34 are adapted for continuous circulation of the solution.

[0028] In system operation, tissue 14 is first located away from optical field 25. Spectrophotometer 18 examines medium 12 in field region 25, and control 35 compares the detected data to the preselected values of the absorption coefficient (μ_a) and the scattering coefficient (μ_s). Next, locator 15 positions tissue 14 into field 25 and spectrophotometer 18 measures the optical properties of tissue 14 and medium 12. From the spectral data collected with and without tissue 14, computer control 35 determines the optical properties of tissue 14.

[0029] In another preferred method of operation, after measuring the optical properties of medium 12, the scattering and absorptive properties of medium 12 are matched by titration to the properties of tissue 14 so that, when inserted into field 25, tissue 14 does not cause perturbation of field 25. After matching the scattering and absorption coefficients of medium 12 to the coefficients of tissue 14, spectrophotometer 18 detects the same data with or without tissue 14. The known titrated values of μ_a^* and μ_s^* are equal to the μ_a and μ_s values of tissue 14. The matching process is performed by first matching μ_a and then μ_s or vice versa.

[0030] The described method is applicable to both in vivo and in vitro tissue examination. Tissue 14 may be a biopsy specimen enclosed in an optically transparent material or a portion of a human finger inserted into medium 12. The wavelength of light used by spectrophotometer 18 is selected depending on the tissue component of interest (e.g., hemoglobin, oxyhemoglobin, glucose, enzymes); it is within the scope of this invention to use multiple wavelengths.

[0031] The present invention envisions the use of different preferred embodiments of optical medium 12. Referring to Fig. 2, a hollow cylinder 42 filled with medium 12 surrounds, for example, a finger 40 and prevents escape of introduced photons. The optical properties, pressure and volume of medium 12 are controlled by system 30 connected to cylinder 42 by tubes 32 and 34. The inside walls of cylinder 42 are made of a pliable, optically transparent barrier 44. After insertion into cylinder 42, barrier 44 fits snugly around the finger. The dimension of inside barrier 44 is such that after finger 40 is withdrawn, medium 12 fills the volume of cylinder 42 completely. This enables both a background measurement of medium 12 and a measurement of finger 40 in medium 12 in the same way as described in connection with Fig. 1. Optical field 25, controlled by the position of input port 19 and detection port 21, is either in transmission or reflection geometry.

[0032] Referring to Fig. 2B, in another embodiment, cylinder 42 is replaced by a set of cylinders 42A, 42B, 42C..., each containing medium 12 in a fluid or solid state with a constant preselected absorption and scattering coefficient. The solid optical medium is titanium oxide, or other scatterer, imbedded in an absorbing, pliable medium such as a gel.

[0033] A human finger is inserted into the individual cylinders, and the optical properties of the inserted finger are measured by spectrophotometer 18. Using the known optical properties of the cylinders and the input port- detection port geometry, the optical properties (i.e., μ_a and μ_s) of the finger can be matched to the properties of one of the cylinders.

[0034] The preferred embodiments of spectrophotometer 18 are a continuous wave spectrometer, a phase modulation spectrometer and a time-resolved spectrometer, all of them described in the above-cited documents.

[0035] System 10 operating with a dual wavelength continuous wave spectrometer is used, for example, as a finger oximeter. As shown in Fig. 2A, the vast majority of photons introduced into finger 40 are prevented to escape by surrounding medium 12. Thus, the introduced photons are either absorbed or reach detection port 21 and are registered by the detector. No error of counting the escaped photons as absorbed occurs. The background spectral data corresponding to each selected value of μ_a^* and μ_s^* of cylinder 42 are stored in the system that can match the values of μ_a and μ_s of the finger and the cylinder for each wavelength. For the continuous wave spectrometer that operates at two wavelengths sensitive to hemoglobin (Hb) and oxyhemoglobin (HbO_2) (e.g., 754nm and 816nm), the hemoglobin saturation (Y) is calculated by taking the ratio of absorption coefficients and using the following equation for the oxygen saturation:

$$Y\,(X100\%) = \frac{38\text{-}18\,\dfrac{\mu_a^{754}}{\mu_a^{816}}}{25\text{+}3\,\dfrac{\mu_a^{754}}{\mu_a^{816}}} \qquad (2)$$

wherein the coefficients are determined from the extinction values of hemoglobin at 754 nm and 816 nm that are $\varepsilon_{Hb} = 0.38\ cm^{-1}\ mM^{-1}$, $\varepsilon_{Hb} = 0.18\ cm^{-1}mM^{-1}$, respectively, and the difference extinction coefficients between oxyhemoglobin and hemoglobin that are $\Delta\varepsilon_{HbO\text{-}Hb} = 0.025\ cm^{-1}\ mM^{-1}$ and $\Delta\varepsilon_{HbO\text{-}Hb} = 0.03\ cm^{-1}\ mM^{-1}$, respectively.

[0036] As known to a person skilled in the art, in the hemoglobin saturation measurement the oximeter normalizes

the detected data to eliminate fluctuations due to the changing blood volume. However, the volume changes can be used to detect the pulse rate.

[0037] Alternatively, a phase modulation spectrometer is used to measure the photon migration by detecting the intensity and the phase shift θ of sinusoidally modulated light introduced at a distance of several centimeters from the detector. For tissue of a small volume, the optimal distance between the input port and the detection port is achieved using optical medium 12. Furthermore, medium 12 substantially eliminates the photon escape.

[0038] The detected phase shift is directly related to the mean of the distribution of photon pathlengths shown in Fig. 2A. Photon migration theory predicts that the detected photons can be represented by a three dimensional "banana-shaped" distribution pattern in the reflection geometry or a "cigar-shaped" distribution pattern in the transmission geometry. Inserting tissue 14 into the center of field 25 causes nonuniformities in the distribution of pathlengths, i.e., the banana-shaped optical field 25 is nonuniform, if the tissue absorption properties are different from the properties of medium 12. If μ_a of the tissue is smaller than that of the surrounding medium, the average pathlength <L> decreases since photons with longer pathlengths are more absorbed and vice versa. Thus, tissue 14 causes changes in the pathlength and the phase shift, θ.

[0039] Furthermore, the detected intensity provides a modulation index (M) that is an important measure of the absorption and scattering properties of a strongly scattering medium. The modulation index is determined as the ratio of the AC amplitude (A^{λ}) to the sum of the AC and DC (DC^{λ}) amplitude.

$$M^{\lambda_1} = \frac{A^{\lambda_1}}{A^{\lambda_1} = DC^{\lambda_1}} \tag{3}$$

[0040] As described in Sevick et al. in Analytical Biochemistry Vol. 195, pp. 330-351, 1991, for low modulation frequencies (i.e., $2\pi f << \mu_a c$) the phase shift is a direct measure of the mean time of flight, <t>, i.e., $\theta \rightarrow 2\pi f<t>$. In a medium wherein all photons travel at a constant speed, c, the phase shift describes the effective, mean pathlength $\theta \rightarrow 2\pi f<L>/c$. Here, all pathlengths are weighted equally. The determined pathlength is used in Beer-Lambert equation for determination of the absorption properties.

[0041] As the modulation frequency increases, the shorter pathlengths become more heavily weighted. At high frequencies (i.e. $2\pi f >> \mu_a c$), the phase shift is no longer a good measure of the distribution of pathlengths and is directly proportional to the absorption coefficient, μ_a, and the effective scattering coefficient, $(1-g)\cdot\mu_s$

$$|\theta^{\lambda}| = a\rho \sqrt{(1-g)\,\mu_s f}\{1 - \frac{\mu_a C}{4\pi f}\} \tag{4}$$

Since the effective scattering coefficient is wavelength independent, ratio of the phase shifts measured at two wavelengths can be written

$$\frac{\theta^{\lambda_1} - \theta_0^{\lambda_1}}{\theta^{\lambda_2} - \theta_0^{\lambda_2}} = \frac{\mu_a^{\lambda_1}}{\mu_a^{\lambda_2}} \tag{5}$$

wherein θ_0^{λ} is the phase shift at the measured wavelength arising from the scattering and background absorption. The ratio of the absorption coefficients is used, for example, for determination of the tissue saturation, Y. A dual frequency, dual wavelength phase modulation spectrometer can be used to determine the saturation by eliminating θ_0. The ratio of absorption coefficients is expressed as a function of the phase shifts measured at different frequencies and wavelengths.

$$\frac{(\theta_{f_1}^{\lambda_1}/\sqrt{f_1}) - (\theta_{f_2}^{\lambda_1}/\sqrt{f_2})}{(\theta_{f_1}^{\lambda_2}/\sqrt{f_1}) - (\theta_{f_2}^{\lambda_2}/\sqrt{f_2})} = \frac{\mu_s^{\lambda_1}}{\mu_s^{\lambda_2}} \tag{6}$$

[0042] In another preferred embodiment, a time-resolved spectrometer (TRS-pulse) introduces, at input port 19, pulses of light on the order of less than a picosecond. Photons traveling through a distribution of migration pathlengths 25 are collected at the detection port 21. The intensity of detected light in the reflectance geometry, R(ρ,t), (or the transmittance geometry T(ρ,d,t)) was determined by solving the diffusion equation in an infinite media as a Green's

function with near infinite boundary conditions. Due to the semi-infinite media condition in the reflectance geometry, the separation of the input and output ports must be on the order of several centimeters to use the following equation.

$$\frac{d}{dt} \log_e R(\rho,t) = \frac{-5}{2t} - \mu_a C + \frac{\rho^2}{4DCt} \tag{7}$$

[0043] For $t \rightarrow \infty$ the absorption coefficient μ_a is determined as

$$\lim_{t\to\infty} \frac{d}{dt} \log_e R(\rho, t) = -\mu_a c \tag{8}$$

wherein ρ is the separation between input and detection ports and c is speed of light in the medium. The effective scattering coefficient (1-g) μ_s is determined as

$$(1-g)\,\mu_s = \frac{1}{\rho^2}\,(4\mu_a c^2 t_{max}^2 + 10 c t_{max}) - \mu_a \tag{9}$$

wherein t_{max} is the delay time at which the detected reflectance time profile ($R(\rho,t) \equiv I(t)$) reaches maximum. The right hand side of Eq. 7 is the decay slope of the arrival time of the modified pulses. The absorption coefficient is quantified by evaluating the decaying slope of the detected pulse, as described in Eq. 7. The effective scattering coefficient, (1-g) $\cdot\mu_s$, is determined from Eq. 8. For the known μ_a and μ_s and the input port, output port geometry, the system has a unique time profile I(t). The stored profile is compared to the time profile detected for the introduced tissue to obtain a difference profile that possesses the scattering and absorption coefficients of tissue 14. Alternatively, μ_a and μ_s of medium 12 and tissue 14 are matched by varying the scattering and absorptive properties of medium 12 so that the detected time profile is not altered by introducing tissue 14.

[0044] The TRS system can be used to calibrate a CW oximeter to quantify the measured data. To account for the difference between the geometric distance (ρ) of the input port and the detection port and the pathlength (<L>), some oximeters use a modified Beer-Lambert equation with a differential pathlength factor (DPF) as follows:

$$absorbance = DPF \cdot \in \cdot [C] \tag{10}$$

However, the differential pathlength factor can not be precisely determined by the CW oximeters since it depends on the pathlength. The TRS determines DPF using the absorption (μ_a) and scattering (μ_s) coefficients as follows:

$$DPF = \frac{\sqrt{3}}{2} \sqrt{\frac{(1-g)\,\mu_s}{\mu_a}} \tag{11}$$

[0045] An alternative embodiment of the escape preventing optical medium used for examining the head of a neonate (46) is an optrode holder 45, shown in Fig. 3. Optical fibers 20 and 22 are projected into a solid scattering material 47, such as styrofoam, which affords a return pathway for escaping photons 48. The pathlength of the migrating photons in the tissue is much longer since the photons return to the tissue by the scattering materials, as shown by the zig-zag arrows 48. Thus, the banana-shaped pattern will penetrate more deeply and meaningful spectroscopic data can be obtained at smaller input-output fiber separations without the danger of photon leakage or "short" by substantially direct pathways.

[0046] Different embodiments of system 10 are adapted to perform either a single measurement or a continuous, time-dependent monitoring of the selected physiological property. Visual display for continuous monitoring of the measured values may be added. Furthermore, a warning signal may be issued when the measured value equals to a preselected value.

EXAMPLE

[0047] Referring to Fig. 4, in a test study, a TRS-pulse spectrophotometer was used for quantitative determination of the scattering and absorptive properties of a human finger. To create semi-infinite boundary conditions, examined

index finger 40 was immersed into a relatively large volume of intralipid solution 52 with carbon containing india ink. A commercially available intralipid of about 20% concentration was diluted to about 0.5%-2.5% concentration to produce surrounding medium 52. The concentration of the intralipid determines the scattering properties of the solution and the amount of the india ink governs the absorptive properties. Selected amounts of the diluted carbon black ink were added into the matching medium according to the needs. In the test, a 1.4 liter cylinder container 51 of about 15 cm in diameter and 8 cm in height was used to hold matching medium 52. Almost all of the measurements were performed on the index finger of twenty five healthy volunteers (male and female) that included Caucasian, Asian, and African-American population. Fiber ends 57 and 59 of optical fibers 56 and 60 inserted into the host medium several millimeters below the solution surface and maintained in a separation of 3 cm on both sides of examined finger 40. Finger 40 was immersed about 5-6 cm below the surface of surrounding medium 52 in a manner to be located in an optical field defined by the immersed ends 57 and 59. This prevented most photons from being transmitted to the surface.

[0048] The dual wavelength TRS system with a 5 MHz repetition rate injected 100-ps pulses (61) of red (670 nm) or near-infrared (750 and 830 nm) light created in pulser 62 into medium 52. Optical input fiber 56 of a 1 μm diameter and optical output fiber 60 of a 2mm diameter were used. The detector consisted of a micro-channel-plate photomultiplier tube 64 (MCP-PMT) with a time resolution of 150 ps connected to a constant fraction discriminator (CFD) 66. The single photon counting system included a time amplitude converter (TAC) 68 and computer 70 for registering digitized data. The TRS measurements were taken both in the absence and in the presence of finger 40.

[0049] The above-described matching method was used by first increasing the absorption coefficient μ_a (h) of surrounding medium 52 by adding the diluted black ink. Once the appropriate absorber concentration was determined, the second titration process was used to determine μ_s' (h) by increasing the concentration of the intralipid.

[0050] The TRS data were deconvoluted with the instrumental function that compensates for the instrument's response. The values of μ_a, μ_s', and T_o (i.e., the laser pulse injection time) were least-square fitted. The absorption coefficient μ_a and the scattering coefficient μ_s' were expressed using $\log_{10}$ base, which can be converted to $\log_e$ base simply by multiplying 2.303. (NOTE: for μ_s calculated by Eq. 9 this conversion cannot be used.)

[0051] Fig. 4A displays the absorption coefficients obtained on fourteen people, (four Caucasian, five Asians, and five African-American) with the matching method and direct measurement, respectively, at 670 nm wavelength and a 2.5 cm interfiber distance. The relative values of μ_a obtained in the matching measurement varied from 0.05 cm^{-1} to 0.08 cm^{-1}, apparently randomly among the three populations; however, the values in the direct measurement varied even more. The direct measurement gives much higher values of μ_a than the values obtained with the matching method which may be due to photon escape from the finger surface when the optical fibers are attached to the measured finger directly. Fig. 4B shows the absorption values measured for a different group of volunteers. Fig. 4C shows the values of μ_a as a function of the number of observations. In this study, no relationship was found between the finger diameter and the absorption coefficients μ_a indicating that the size of the finger has no effect on μ_a.

[0052] Fig. 4D display μ_s at measured 670 nm by the matching method for the fourteen individuals of Fig. 4A. The scattering data are summarized in Fig. 4E as a function of the relative occurrence of μ_s. The mean value is 6.26 cm^{-1} and the standard error is 0.64 cm^{-1} with an approximately gaussian distribution.

[0053] The quantitative hemoglobin saturation of the finger was measured at 670 nm and 750 nm. Since the contribution of water absorption at 750 nm is relatively high, it was necessary to subtract water absorption background from the calculated value of μ_a. For this purpose, we assumed the absorption coefficients of water at 750 nm and 670 nm equal to 0.004 1/cm and 0.026 1/cm, respectively. The background corrected values of μ_a and the corresponding hemoglobin saturation values are shown in the following table and plotted in Figs. 4F and 4G.

Subject	μ_a^{670} (1/cm)	μ_a^{750} (1/cm)	μ_a^{670}/μ_a^{750}	Y (%)
1	0.05119	0.04453	1.14948	83.88
2	0.0467	0.04386	1.0647	87.47
3	0.0578	0.04424	1.30663	76.20
4	0.06276	0.05204	1.20588	81.29
5	0.05743	0.04286	1.339860	74.38
6	0.05045	0.04275	1.18023	82.49
7	0.05936	0.05234	1.13417	84.55
8	0.0493	0.04187	1.17756	82.61
9	0.05488	0.0513	1.06981	87.26

(continued)

Subject	μ_a^{670} (1/cm)	μ_a^{750} (1/cm)	μ_a^{670}/μ_a^{750}	Y (%)
10	0.05012	0.0457	1.09662	86.16
11	0.05992	0.04895	1.22418	80.41
12	0.04848	0.04492	1.07935	86.87
13	0.05206	0.05207	0.99973	90.01
14	0.6463	0.05608	1.15249	83.74

Claims

1. A spectrophotometric method of examination of an object of interest using visible or infra-red radiation introduced to optical paths passing through the object, said method comprising the steps of:

   (a) providing, at said object, optical means for limiting escape of photons and providing return paths for photons escaped from inside to outside of said object,
   (b) introducing into the object, at an optical input port, electromagnetic radiation of a selected wavelength in the visible or infra-red range, photons of said radiation migrating inside of said object,
   (c) detecting photons of said radiation that has migrated in said object from said input port to an optical detection port, the detected radiation also including photons that returned from outside of said object into said object, and
   (d) determining an optical property of said object based on the changes of properties of the introduced and the detected radiation.

2. The spectrophotometric method of claim 1, wherein said object is biological tissue of a relatively small volume, said biological tissue occupying a part of said optical paths between said optical input port and said optical detection port and thereby creating a tissue-medium optical path.

3. The spectrophotometric method of claim 1 or 2, wherein said optical means comprise an optical medium at least partially surrounding said object, said optical medium having selectable optical property.

4. The spectrophotometric method of claim 1 or 2, wherein said optical means comprise an optical medium at least partially surrounding said object, said medium having at least one optical property substantially matched to the optical property of said object.

5. The spectrophotometric method of claim 3 or 4, wherein said optical property of said optical medium is an absorption coefficient or a scattering coefficient.

6. The spectrophotometric method of any preceding claim, wherein said determining step (d) comprises:

   (e) selecting optical means comprising an optical medium with at least one optical property comparable to the optical property of said object,
   (f) measuring the optical property of said object by performing said (b) and (c) steps,
   (g) selecting another optical means comprising an optical medium with at least one optical property matched closer to the corresponding optical property of said object, and
   (h) repeating iteratively said (f) and (g) steps until the optical property of said optical medium is substantially matched to the optical property of said object.

7. The spectrophotometric method of any of claims 1 to 5, wherein said determining step comprises:

   (e) introducing known changes in the scattering property or the absorptive property of said optical medium,
   (f) measuring the optical property of said object by performing said (b) and (c) steps,
   (g) introducing additional known changes in the scattering property or the absorptive property of said optical medium to approximate at least one said property to the optical property of said object, and
   (h) repeating iteratively said (f) and (g) steps until at least one of said optical properties of said optical medium

is substantially matched to the corresponding optical property of said object.

8. The spectrophotometric method of any preceding claim, wherein said radiation of said selected wavelength is one of the following types of radiation: a continuous wave radiation, a continuous wave radiation modulated by a carrier waveform of a frequency on the order of 10^8 Hz or radiation of pulses having duration on the order of a nanosecond or less.

9. The spectrophotometric method of any preceding claim, performed in vivo wherein said object is biological tissue and said optical property is related to hemoglobin oxygenation, glucose or enzyme levels in said tissue.

10. The spectrophotometric method of any of claims 1 to 8, wherein said object is a human finger, the head or a biopsy specimen.

11. A spectrophotometric system (10) for examination of an object (14, 40, 46) of interest using visible or infra-red radiation introduced to optical paths passing through the object, said system comprising:

a spectrophotometer unit (18) including a light source (18A, 62) optically connected to an optical input port (19, 57) adapted to introduce photons of said radiation into the object, the introduced photons migrating inside of said object, and a light detector (23, 64) optically connected to an optical detection port (21, 59) adapted to detect radiation that has migrated over optical paths in the object,
optical means (12, 45) arranged at the object of interest and adapted to limit escape of the introduced photons and provide return paths for photons (25, 48) escaped from inside to outside of the object,
processing means (35), connected to said spectrophotometer unit, adapted to determine an optical property of the object based on the changes between the introduced and the detected radiation, the detected radiation also including photons that returned from outside of said object into said object.

12. The spectrophotometric system of claim 11, wherein said object is biological tissue (14, 40) of a small volume, said biological tissue occupying a part of an optical path between said optical input port and said optical detection port and thereby creating a tissue-medium optical path.

13. The spectrophotometric system of claim 11 or 12, wherein said optical means comprise an optical medium (12), at least partially surrounding said object, having a selectable optical property.

14. The spectrophotometric system of claim 11 or 12, wherein said optical means comprise an optical medium (12) at least partially surrounding said object, said optical medium having at least one optical property substantially matched to the corresponding optical property of said object.

15. The spectrophotometric system of claim 13 or 14, wherein said optical medium includes a fluid or a solid.

16. The spectrophotometric system of any of claims 11 to 15, wherein said determined optical property of the object is an absorption coefficient or a scattering coefficient.

17. The spectrophotometric system of any of claims 11 to 16, further comprising another optical medium with different scattering or absorptive properties approximating the scattering or absorptive properties of said object.

18. The spectrophotometric system of any of claims 11 to 17, wherein said object is biological tissue and said determined optical property is related to hemoglobin oxygenation, glucose or enzyme levels in said tissue.

19. The spectrophotometric system of any of claims 11 to 18, wherein said object is a human finger, the head or a biopsy specimen.

20. The spectrophotometric system of any of claims 11 to 19, wherein said spectrophotometer unit (18) is a continuous wave spectrophotometer.

21. The spectrophotometric system of any of claims 11 to 19, wherein said spectrophotometer unit is a phase modulation spectrophotometer and said introduced radiation is modulated by a carrier waveform of a frequency on the order of 10^8 Hz.

22. The spectrophotometric system of any of claims 11 to 19, wherein said spectrophotometer unit is a time resolved spectrophotometer and said introduced radiation comprises radiation pulses on the order of a nanosecond or less.

Patentansprüche

1. Spektrophotometrisches Verfahren zur Untersuchung eines Zielobjekts unter Verwendung von sichtbarer oder Infrarot-Strahlung, die in durch das Objekt führende optische Wege eingeführt wird, wobei das Verfahren die folgenden Schritte umfaßt:

   (a) Bereitstellen von optischen Mitteln an dem Objekt zur Begrenzung des Austritts von Photonen und Bereitstellen von Rückwegen für Photonen, die aus dem Inneren in den Bereich außerhalb des Objektes ausgetreten sind,

   (b) Einführen von elektromagnetischer Strahlung mit einer ausgewählten Wellenlänge im sichtbaren oder Infrarot-Bereich an einer optischen Eingangsöffnung in das Objekt, wobei Photonen der Strahlung in das Objekt hineinwandern,

   (c) Detektieren von Photonen der Strahlung, die von der Eingangsöffnung zu einer optischen Detektionsöffnung in dem Objekt gewandert ist, wobei die detektierte Strahlung auch Photonen umfaßt, die aus dem Bereich außerhalb des Objekts in das Objekt zurückgekehrt sind, und

   (d) Bestimmen einer optischen Eigenschaft des Objekts auf Grundlage der Eigenschaftsveränderungen der eingeführten und der detektierten Strahlung.

2. Spektrophotometrisches Verfahren nach Anspruch 1, wobei das Objekt biologisches Gewebe mit relativ geringem Volumen ist, wobei das biologische Gewebe einen Teil des optischen Weges zwischen der optischen Eingangsöffnung und der optischen Detektionsöffnung einnimmt und dadurch einen optischen Weg aus Gewebe und Medium erzeugt.

3. Spektrophotometrisches Verfahren nach Anspruch 1 oder 2, wobei die optischen Mittel ein optisches Medium umfassen, das das Objekt zumindest teilweise umgibt, wobei das optische Medium wählbare optische Eigenschaften aufweist.

4. Spektrophotometrisches Verfahren nach Anspruch 1 oder 2, wobei die optischen Mittel ein optisches Medium umfassen, das das Objekt zumindest teilweise umgibt, wobei das Medium zumindest eine optische Eigenschaft aufweist, die im wesentlichen auf die optische Eigenschaft des Objekts abgestimmt ist.

5. Spektrophotometrisches Verfahren nach Anspruch 3 oder 4, wobei die optische Eigenschaft des optischen Mediums ein Absorptionskoeffizient oder ein Streukoeffizient ist.

6. Spektrophotometrisches Verfahren nach einem der vorstehenden Ansprüche, wobei der Bestimmungsschritt (d) folgende Schritte umfaßt:

   (e) Auswählen von optischen Mitteln, die ein optisches Medium mit mindestens einer mit der optischen Eigenschaft des Objekts vergleichbaren optischen Eigenschaft umfassen,

   (f) Messen der optischen Eigenschaft des Objekts durch Durchführen der Schritte (b) und (c),

   (g) Auswählen eines anderen optischen Mittels, das ein optisches Medium mit mindestens einer optischen Eigenschaft umfaßt, die besser auf die korrespondierende optische Eigenschaft des Objekts abgestimmt ist, und

   (h) iteratives Wiederholen der Schritte (f) und (g) bis die optische Eigenschaft des optischen Mediums im Wesentlichen auf die optische Eigenschafts des Objekts abgestimmt ist.

7. Spektrophotometrisches Verfahren nach einem der Ansprüche 1 bis 5, wobei der Bestimmungsschritt folgende Schritte umfaßt:

(e) Einführen bekannter Veränderungen in die Streueigenschaft oder die Absorptionseigenschaft des optischen Mediums,

(f) Messen der optischen Eigenschaft des Objekts durch Durchführung der Schritte (b) und (c),

(g) Einführen zusätzlicher bekannter Veränderungen in die Streueigenschaft oder die Absorptionseigenschaft des optischen Mediums, um mindestens eine der Eigenschaften an die optische Eigenschaft des Objekts anzunähern, und

(h) iteratives Wiederholen der Schritte (f) und (g) bis mindestens eine der optischen Eigenschaften des optischen Mediums im wesentlichen auf die korrespondierende optische Eigenschaft des Objekts abgestimmt ist.

8. Spektrophotometrisches Verfahren nach einem der vorstehenden Ansprüche, wobei die Strahlung mit der ausgewählten Wellenlänge eine der folgenden Strahlungstypen ist: eine Dauerstrichstrahlung, eine Dauerstrichstrahlung, die durch eine Trägerwellenform mit einer Frequenz in der Größenordnung von 10^8 Hz moduliert ist oder Pulsstrahlung mit einer Dauer in der Größenordnung einer Nanosekunde oder weniger.

9. Spektrophotometrisches Verfahren nach einem der vorstehenden Ansprüche, das in vivo durchgeführt wird, wobei das Objekt biologisches Gewebe ist und die optische Eigenschaft auf die Hämoglobinoxygenierung, die Glucose- oder die Enzymniveaus in dem Gewebe bezogen ist.

10. Spektrophotometrisches Verfahren nach einem der Ansprüche 1 bis 8, wobei das Objekt ein menschlicher Finger, der Kopf oder eine Biopsieprobe ist.

11. Spektrophotometrisches System (10) zur Untersuchung eines Zielobjekts (14, 40, 46) unter Verwendung von sichtbarer oder Infrarot-Strahlung, die in durch das Objekt führende optische Wege eingeführt wird, mit

einer Spektrophotometereinheit (18) mit einer Lichtquelle (18A, 62), die optisch mit einer optischen Eingangsöffnung (19, 57) verbunden ist, die dazu ausgelegt ist, Photonen der Strahlung in das Objekt einzuführen, wobei die eingeführten Photonen in das Objekt hineinwandern, und mit einem Lichtdetektor (23, 64), der optisch mit einer optischen Detektionsöffnung (21, 59) verbunden ist, die dazu ausgelegt ist, die über optische Wege in dem Objekt gewanderte Strahlung zu detektieren,

optischen Mitteln (12, 45), die an dem Zielobjekt angeordnet sind und dazu ausgelegt sind, den Austritt der eingeführten Photonen zu begrenzen und Rückwege für Photonen (25, 48) zur Verfügung zu stellen, die aus dem Inneren in den Bereich außerhalb des Objekts ausgetreten sind,

Verarbeitungsmitteln (35), die mit der Spektrophotometereinheit verbunden sind und dazu ausgelegt sind, eine optische Eigenschaft des Objekts auf Grundlage der Veränderungen zwischen der eingeführten und der detektierten Strahlung zu bestimmen, wobei die detektierte Strahlung auch Photonen umfaßt, die von dem Bereich außerhalb des Objekts in das Objekt zurückgekehrt sind.

12. Spektrophotometrisches System nach Anspruch 11, wobei das Objekt biologisches Gewebe (14, 40) mit einem geringen Volumen ist, wobei das biologische Gewebe einen Teil eines optischen Weges zwischen der optischen Eingangsöffnung und der optischen Detektionsöffnung einnimmt und dadurch einen optischen Weg aus Gewebe und Medium erzeugt.

13. Spektrophotometrisches System nach Anspruch 11 oder 12, wobei die optischen Mittel ein optisches Medium (12) umfassen, das das Objekt zumindest teilweise umgibt und das eine wählbare optische Eigenschaft aufweist.

14. Spektrophotometrisches System nach Anspruch 11 oder 12, wobei die optischen Mittel ein optisches Medium (12) umfassen, das das Objekt zumindest teilweise umgibt, wobei das optische Medium mindestens eine optische Eigenschaft aufweist, die im wesentlichen auf die korrespondierende optische Eigenschaft des Objekts abgestimmt ist.

15. Spektrophotometrisches System nach Anspruch 13 oder 14, wobei das optische Medium ein Fluid oder einen Feststoff umfaßt.

16. Spektrophotometrisches System nach einem der Ansprüche 11 bis 15, wobei die untersuchte optische Eigenschaft des Objekts ein Absorptionskoeffizient oder ein Streukoeffizient ist.

17. Spektrophotometrisches System nach einem der Ansprüche 11 bis 16, das des weiteren ein anderes optisches Medium mit unterschiedlichen Streu- oder Absorptionseigenschaften umfaßt, die sich den Streu- oder Absorptionseigenschaften des Objekts annähern.

18. Spektrophotometrisches System nach einem der Ansprüche 11 bis 17, wobei das Objekt ein biologisches Gewebe ist und die untersuchte optische Eigenschaft auf die Hämoglobinoxygenierung, die Glucose oder die Enzymniveaus in dem Gewebe bezogen ist.

19. Spektrophotometrisches System nach einem der Ansprüche 11 bis 18, wobei das Objekt ein menschlicher Finger, der Kopf oder eine Biopsieprobe ist.

20. Spektrophotometrisches System nach einem der Ansprüche 11 bis 19, wobei die Spektrophotometereinheit (18) ein Dauerstrich-Spektrophotometer ist.

21. Spektrophotometrisches System nach einem der Ansprüche 11 bis 19, wobei die Spektrophotometereinheit ein Phasenmodulationsspektrophotometer ist und die eingeführte Strahlung durch eine Trägerwellenform mit einer Frequenz in der Größenordnung von 10^8 Hz moduliert wird.

22. Spektrophotometrisches System nach einem der Ansprüche 11 bis 19, wobei die Spektrophotometereinheit ein zeitaufgelöstes Spektrophotometer ist und die eingeführte Strahlung Strahlungsimpulse in der Größenordnung einer Nanosekunde oder weniger aufweist.

Revendications

1. Procédé spectrophotométrique d'examen d'un objet à examiner utilisant un rayonnement visible ou infrarouge introduit dans des trajets optiques traversant l'objet, ledit procédé comprenant les étapes consistant à :

   (a) disposer, au niveau dudit objet, des moyens optiques pour limiter la fuite de photons et disposer des trajets de retour pour les photons échappés de l'intérieur vers l'extérieur dudit objet,
   (b) introduire dans l'objet, au niveau d'un orifice d'entrée optique, un rayonnement électromagnétique d'une longueur d'onde sélectionnée dans l'intervalle visible ou infrarouge, les photons dudit rayonnement migrant à l'intérieur dudit objet,
   (c) détecter les photons dudit rayonnement qui ont migré dans ledit objet depuis ledit orifice d'entrée vers un orifice de détection optique, le rayonnement détecté comprenant également les photons qui sont retournés de l'extérieur dudit objet dans ledit objet, et
   (d) déterminer une propriété optique dudit objet sur la base des modifications entre les propriétés du rayonnement introduit et détecté.

2. Procédé spectrophotométrique selon la revendication 1, dans lequel ledit objet est un tissu biologique de volume relativement petit, ledit tissu biologique occupant une partie desdits trajets optiques entre ledit orifice d'entrée optique et ledit orifice de détection optique et créant ainsi un trajet optique tissu-milieu.

3. Procédé spectrophotométrique selon la revendication 1 ou 2, dans lequel ledit moyen optique comprend un milieu optique entourant au moins partiellement ledit objet, ledit milieu optique ayant une propriété optique pouvant être sélectionnée.

4. Procédé spectrophotométrique selon la revendication 1 ou 2, dans lequel ledit moyen optique comprend un milieu optique entourant au moins partiellement ledit objet, ledit milieu ayant au moins une propriété optique correspondant sensiblement à la propriété optique dudit objet.

5. Procédé spectrophotométrique selon la revendication 3 ou 4, dans lequel ladite propriété optique dudit milieu optique est un coefficient d'absorption ou un coefficient de dispersion.

6. Procédé spectrophotométrique selon l'une quelconque des revendications précédentes, dans lequel ladite étape

de détermination (d) comprend les étapes consistant à :

(e) sélectionner des moyens optiques comprenant un milieu optique ayant au moins une propriété optique comparable à la propriété optique dudit objet,
(f) mesurer la propriété optique dudit objet en conduisant lesdites étapes (b) et (c),
(g) sélectionner un autre moyen optique comprenant un milieu optique ayant au moins une propriété optique plus proche de la propriété optique correspondante dudit objet, et
(h) répéter par itération lesdites étapes (f) et (g) jusqu'à ce que la propriété optique dudit milieu optique corresponde sensiblement à la propriété optique dudit objet.

7. Procédé spectrophotométrique selon l'une quelconque des revendications 1 à 5, dans lequel ladite étape de détermination comprend les étapes consistant à :

(e) apporter des modifications connues à la propriété de dispersion ou à la propriété d'absorption dudit milieu optique,
(f) mesurer la propriété optique dudit objet en conduisant lesdites étapes (b) et (c),
(g) apporter des modifications connues à la propriété de dispersion ou à la propriété d'absorption dudit milieu optique pour approcher par approximation ladite au moins une propriété de la propriété optique dudit objet, et
(h) répéter par itération lesdites étapes (f) et (g) jusqu'à ce qu'au moins une desdites propriétés optiques dudit milieu optique corresponde sensiblement à la propriété optique correspondante dudit objet.

8. Procédé spectrophotométrique selon l'une quelconque des revendications précédentes, dans lequel ledit rayonnement de ladite longueur d'onde sélectionnée est d'un des types de rayonnement suivants : un rayonnement à ondes entretenues, un rayonnement à ondes entretenues modulé par une forme d'onde porteuse d'une fréquence de l'ordre de 10^8 Hz ou un rayonnement d'impulsions ayant une durée d'une nanoseconde ou moins.

9. Procédé spectrophotométrique selon l'une quelconque des revendications précédentes, conduit in vivo dans laquelle ledit objet est un tissu biologique et ladite propriété optique concerne des taux d'oxygénation d'hémoglobine, de glucose ou d'enzyme dans ledit tissu.

10. Procédé spectrophotométrique selon l'une quelconque des revendications 1 à 8, dans lequel ledit objet est un doigt humain, la tête ou un spécimen de biopsie.

11. Système spectrophotométrique (10) pour l'examen d'un objet (14, 40, 46) à examiner utilisant un rayonnement visible ou infrarouge introduit dans des trajets optiques traversant l'objet, ledit système comprenant :

une unité spectrophotométrique (10) comprenant une source de lumière (18A, 62) optiquement connectée à un orifice d'entrée optique (19, 57) adapté pour introduire des photons dudit rayonnement dans l'objet, les photons introduits migrant à l'intérieur dudit objet, et un détecteur de lumière (23, 64) optiquement connecté à un orifice de détection optique (21, 59) adapté pour détecter le rayonnement qui a migré le long des trajets optiques dans l'objet,
des moyens optiques (12, 45) agencés au niveau de l'objet à examiner et adapté pour limiter la fuite de photons et disposer des trajets de retour pour les photons (25, 48) échappés de l'intérieur vers l'extérieur dudit objet,
des moyens de traitement (35) connectés à ladite unité spectrophotométrique, adaptés pour déterminer une propriété optique dudit objet sur la base des variations entre les rayonnements introduits et détectés, le rayonnement détecté comprenant également des photons qui sont retournés de l'extérieur dudit objet dans ledit objet.

12. Système spectrophotométrique selon la revendication 11, dans lequel ledit objet est un tissu biologique (14, 40) de petit volume, ledit tissu biologique occupant une partie d'un trajet optique entre ledit orifice d'entrée optique et ledit orifice de détection optique et créant ainsi un trajet optique tissu-milieu.

13. Système spectrophotométrique selon la revendication 11 ou 12, dans lequel ledit moyen optique comprend un milieu optique (12), entourant au moins partiellement ledit objet, ayant une propriété optique pouvant être sélectionnée.

14. Système spectrophotométrique selon la revendication 11 ou 12, dans lequel ledit moyen optique comprend un milieu optique (12), entourant au moins partiellement ledit objet, ledit milieu optique ayant au moins une propriété

optique qui correspond sensiblement à la propriété optique correspondante dudit objet.

15. Système spectrophotométrique selon la revendication 13 ou 14, dans lequel ledit milieu optique comprend un liquide ou un solide.

16. Système spectrophotométrique selon l'une quelconque des revendications 11 à 15, dans lequel ladite propriété optique déterminée de l'objet est un coefficient d'absorption ou un coefficient de dispersion.

17. Système spectrophotométrique selon l'une quelconque des revendications 11 à 16, comprenant également un autre milieu optique ayant des propriétés de dispersion ou d'absorption différentes approchant par approximation les propriétés de dispersion ou d'absorption dudit objet.

18. Système spectrophotométrique selon l'une quelconque des revendications 11 à 17, dans lequel ledit objet est un tissu biologique et ladite propriété optique déterminée concerne des taux d'oxygénation d'hémoglobine, de glucose ou d'enzyme dans ledit tissu.

19. Système spectrophotométrique selon l'une quelconque des revendications 11 à 18, dans lequel ledit objet est un doigt humain, la tête ou un spécimen de biopsie.

20. Système spectrophotométrique selon l'une quelconque des revendications 11 à 19, dans lequel ladite unité spectrophotométrique (18) est un spectrophotomètre à ondes entretenues.

21. Système spectrophotométrique selon l'une quelconque des revendications 11 à 19, dans lequel ladite unité spectrophotométrique est un spectrophotomètre à modulation de phase et ledit rayonnement introduit est modulé par une forme d'onde porteuse d'une fréquence de l'ordre de 10^8 Hz.

22. Système spectrophotométrique selon l'une quelconque des revendications 11 à 19, dans lequel ladite unité spectrophotométrique est un spectrophotomètre à résolution dans le temps et ledit rayonnement introduit comprend des impulsions de rayonnement de l'ordre d'une nanoseconde ou moins.

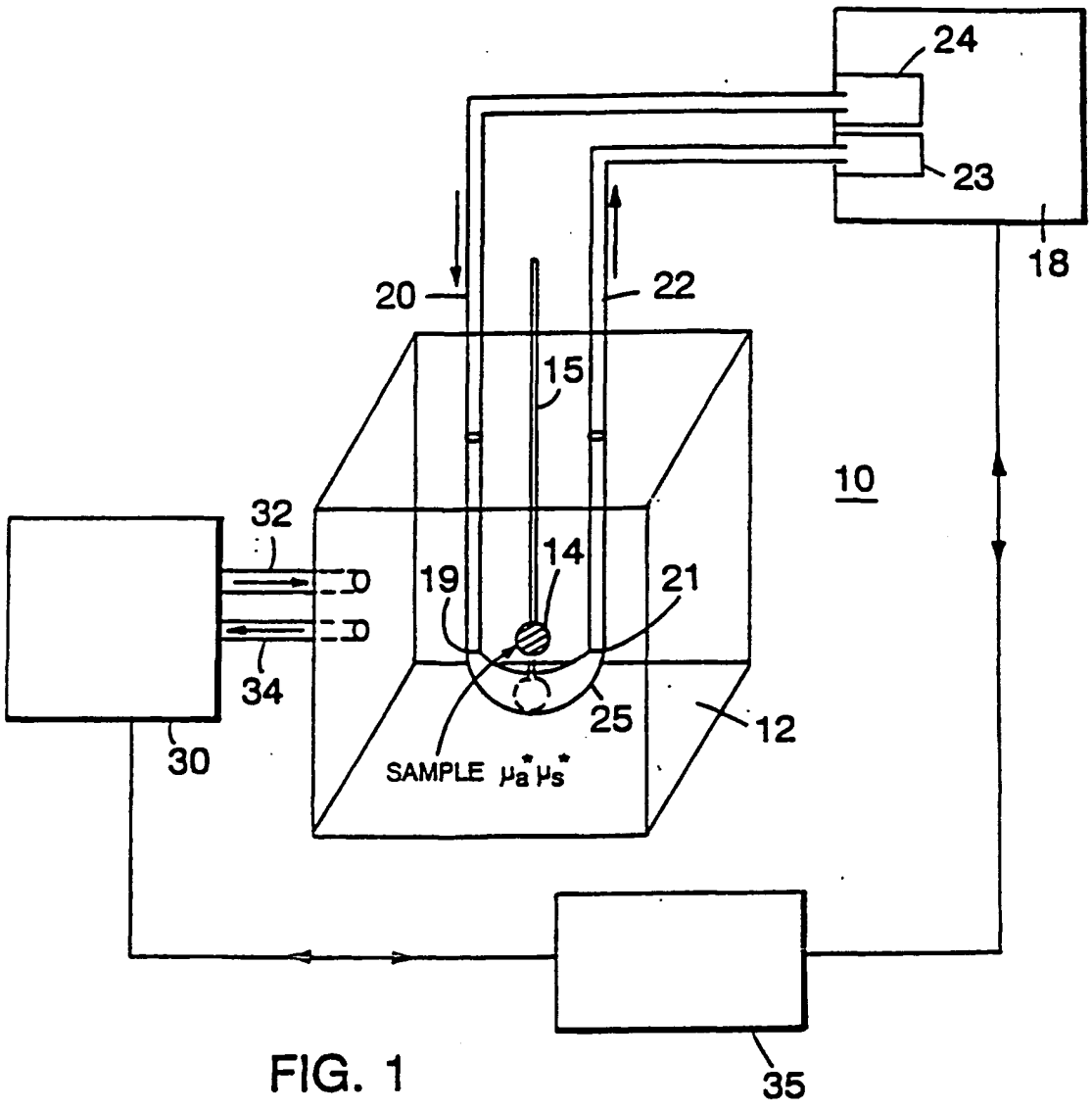


FIG. 1

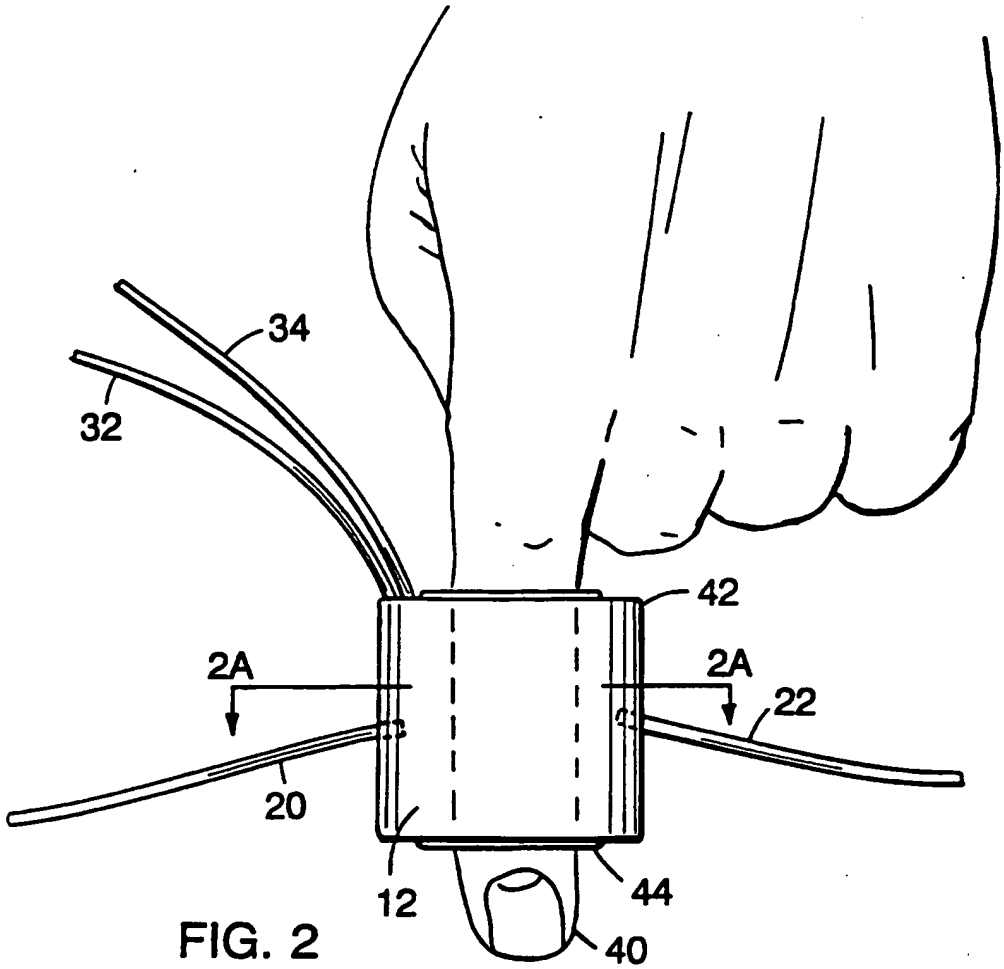


FIG. 2

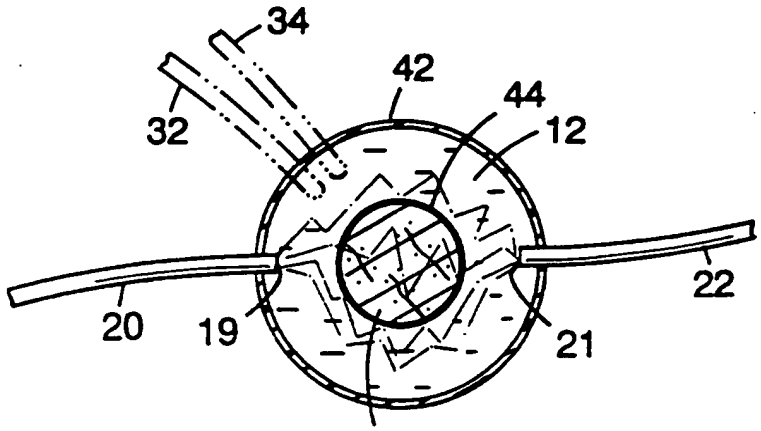


FIG. 2A

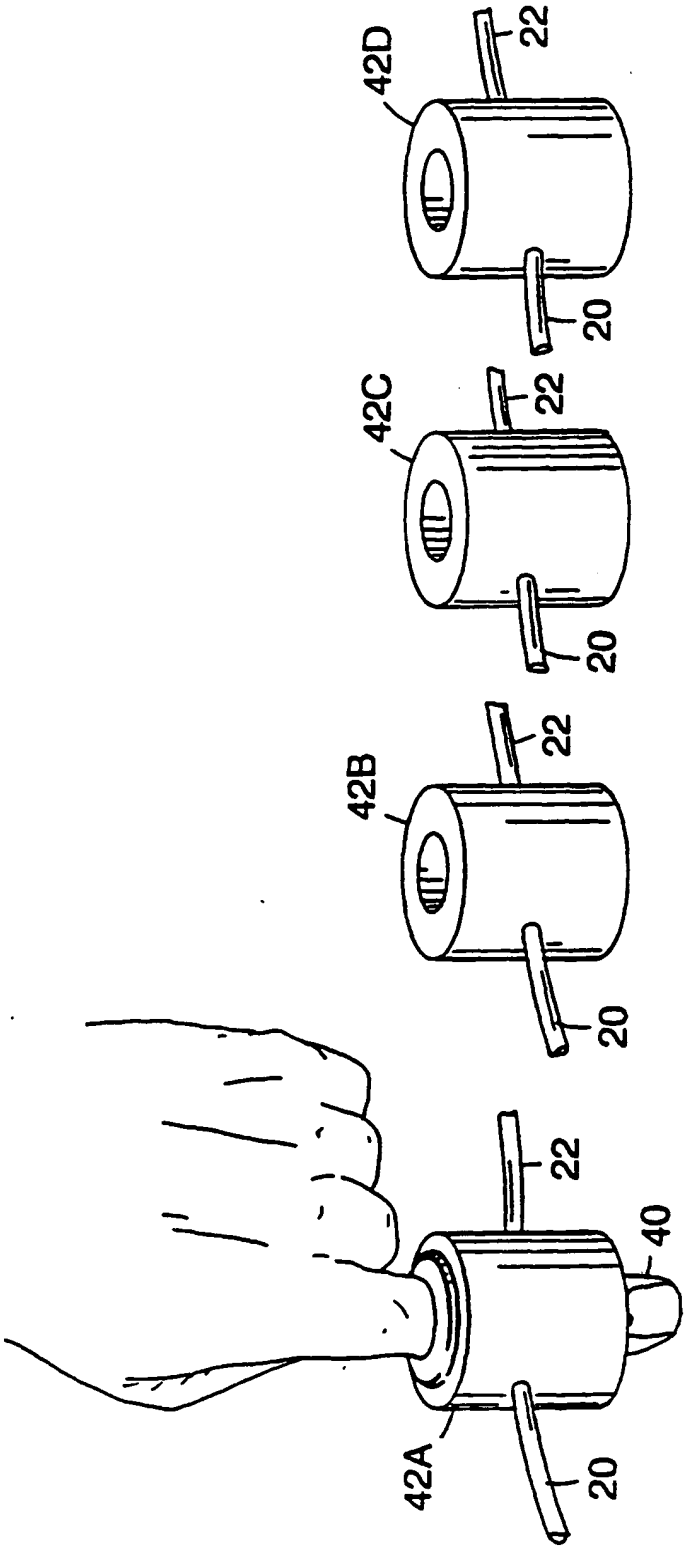
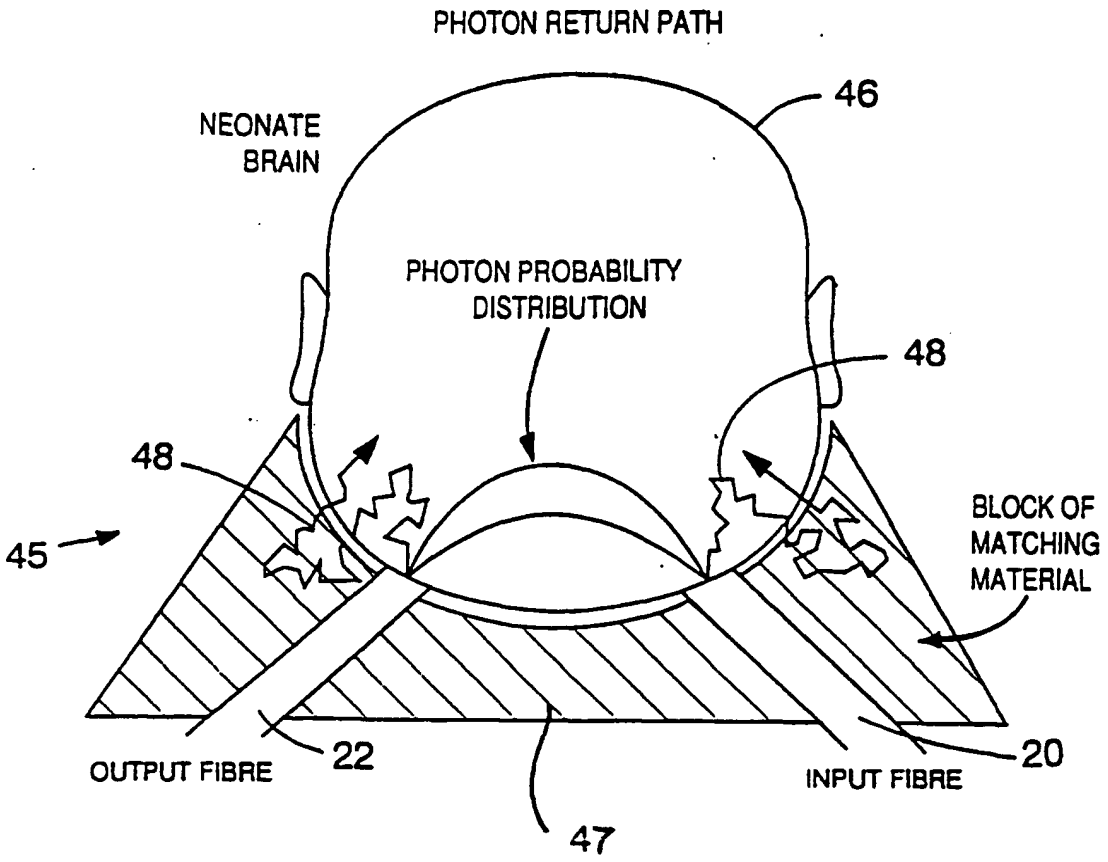


FIG. 2B

FIG. 3


PHOTON RETURN PATH
NEONATE BRAIN
46
PHOTON PROBABILITY DISTRIBUTION
48
48
45
BLOCK OF MATCHING MATERIAL
OUTPUT FIBRE
22
47
INPUT FIBRE
20

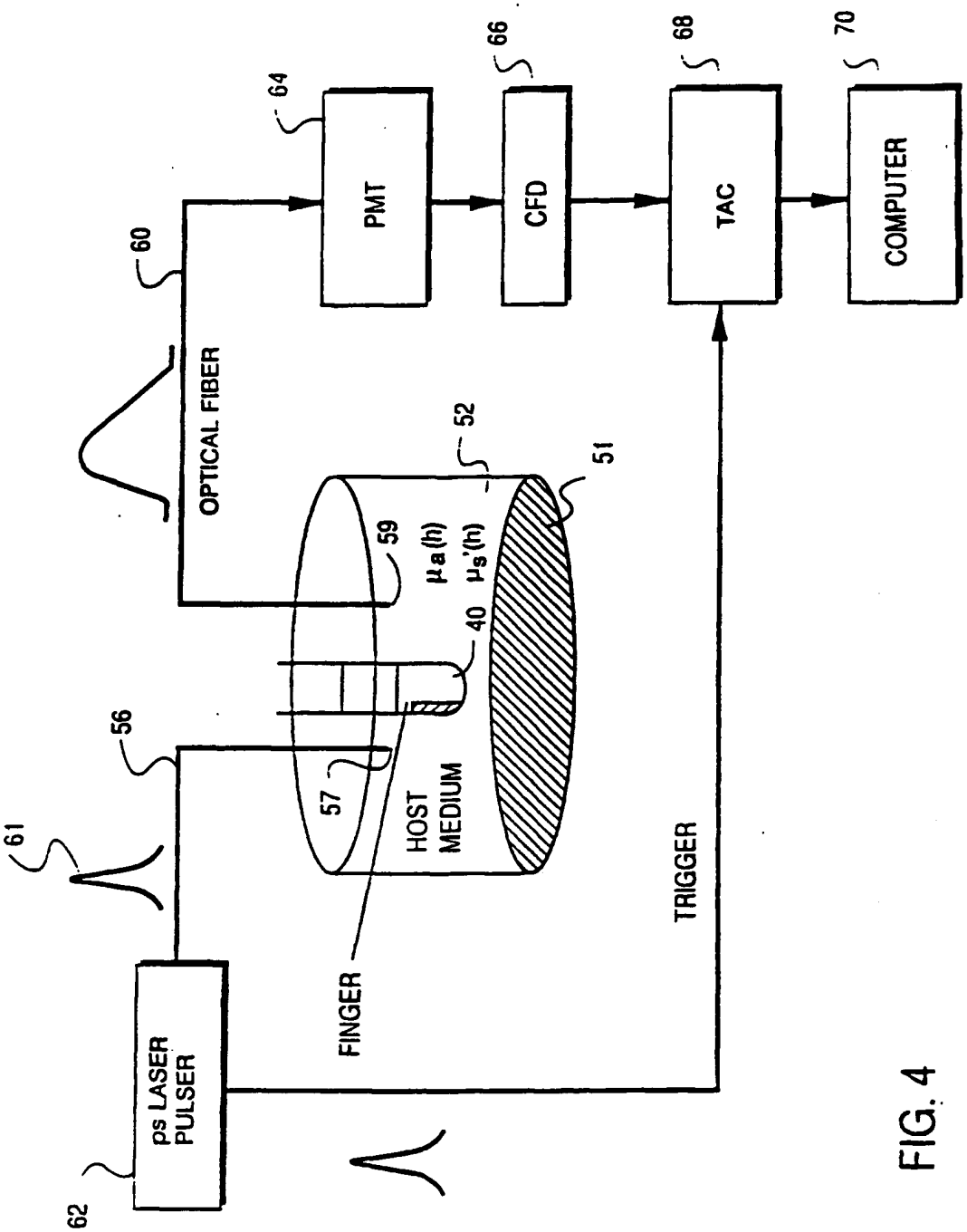

62
ps LASER PULSER
61
56
57
FINGER
HOST MEDIUM
59
$\mu_a(h)$
$\mu_s'(h)$
40
52
51
60
OPTICAL FIBER
64
PMT
66
CFD
68
TAC
70
COMPUTER
TRIGGER

FIG. 4

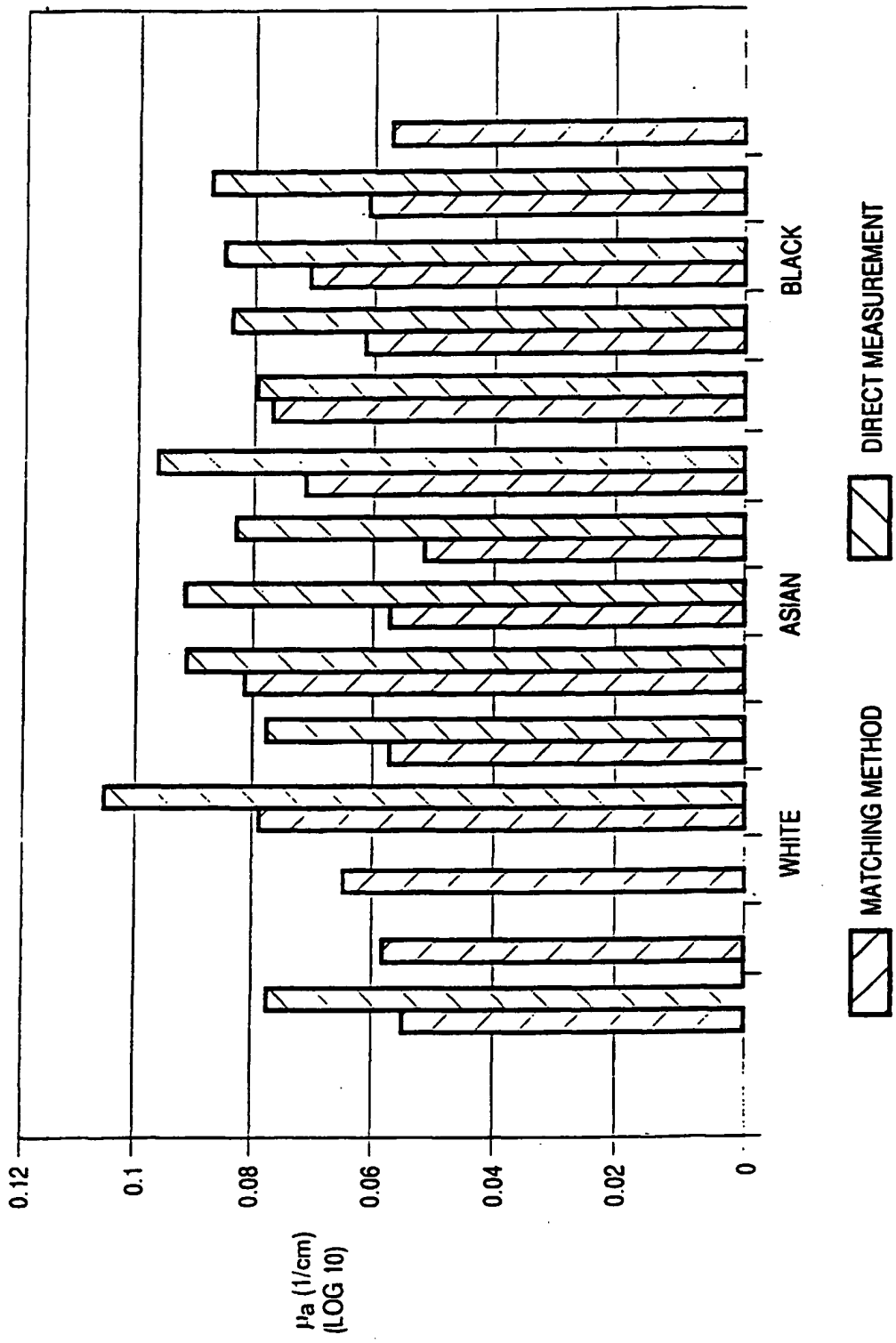
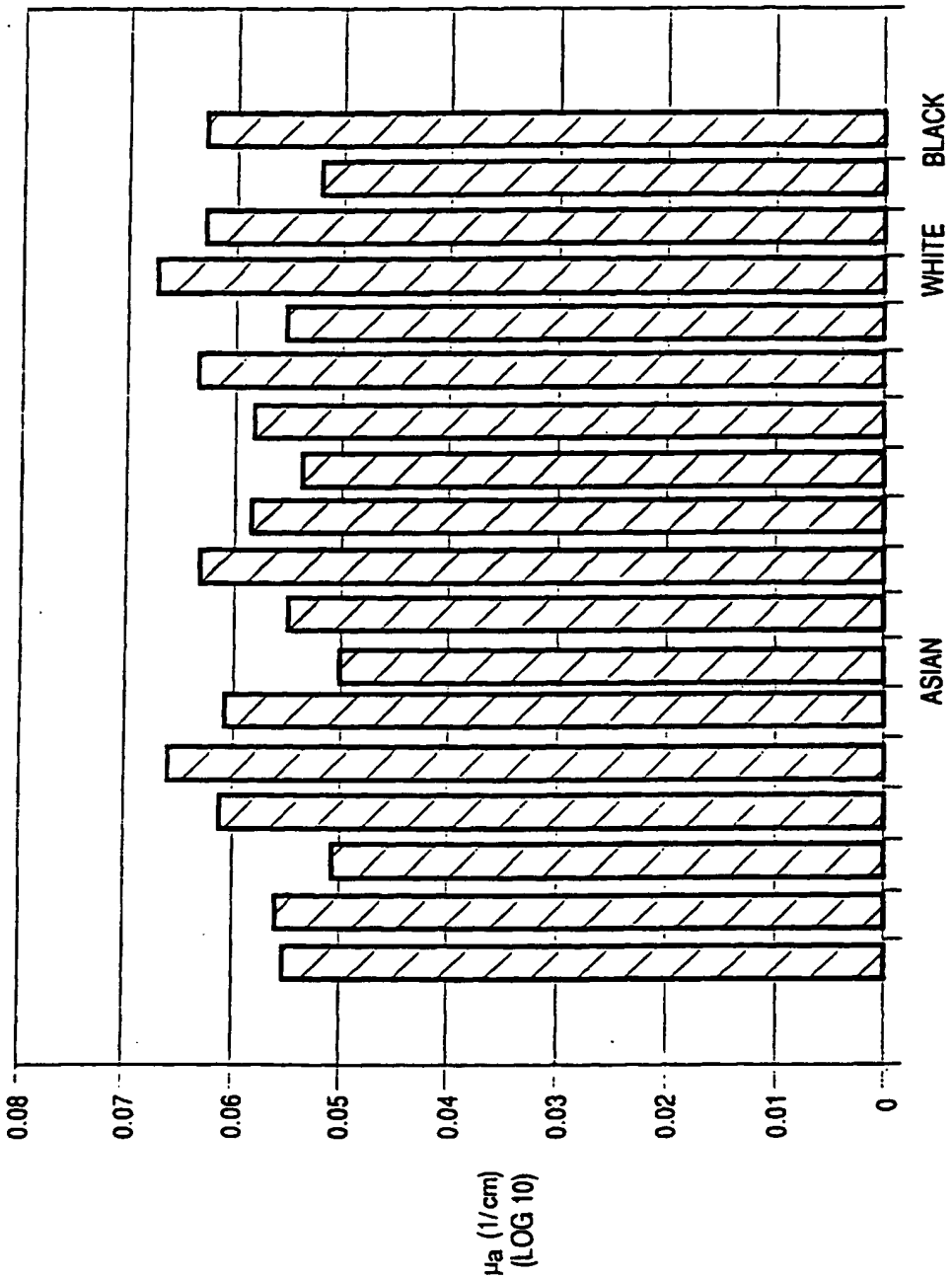

0.12
0.1
0.08
0.06
0.04
0.02
0
μa (1/cm)
(LOG 10)
WHITE
ASIAN
BLACK
MATCHING METHOD
DIRECT MEASUREMENT

FIG. 4A

FIG. 4B


0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
μa (1/cm)
(LOG 10)
ASIAN
WHITE
BLACK

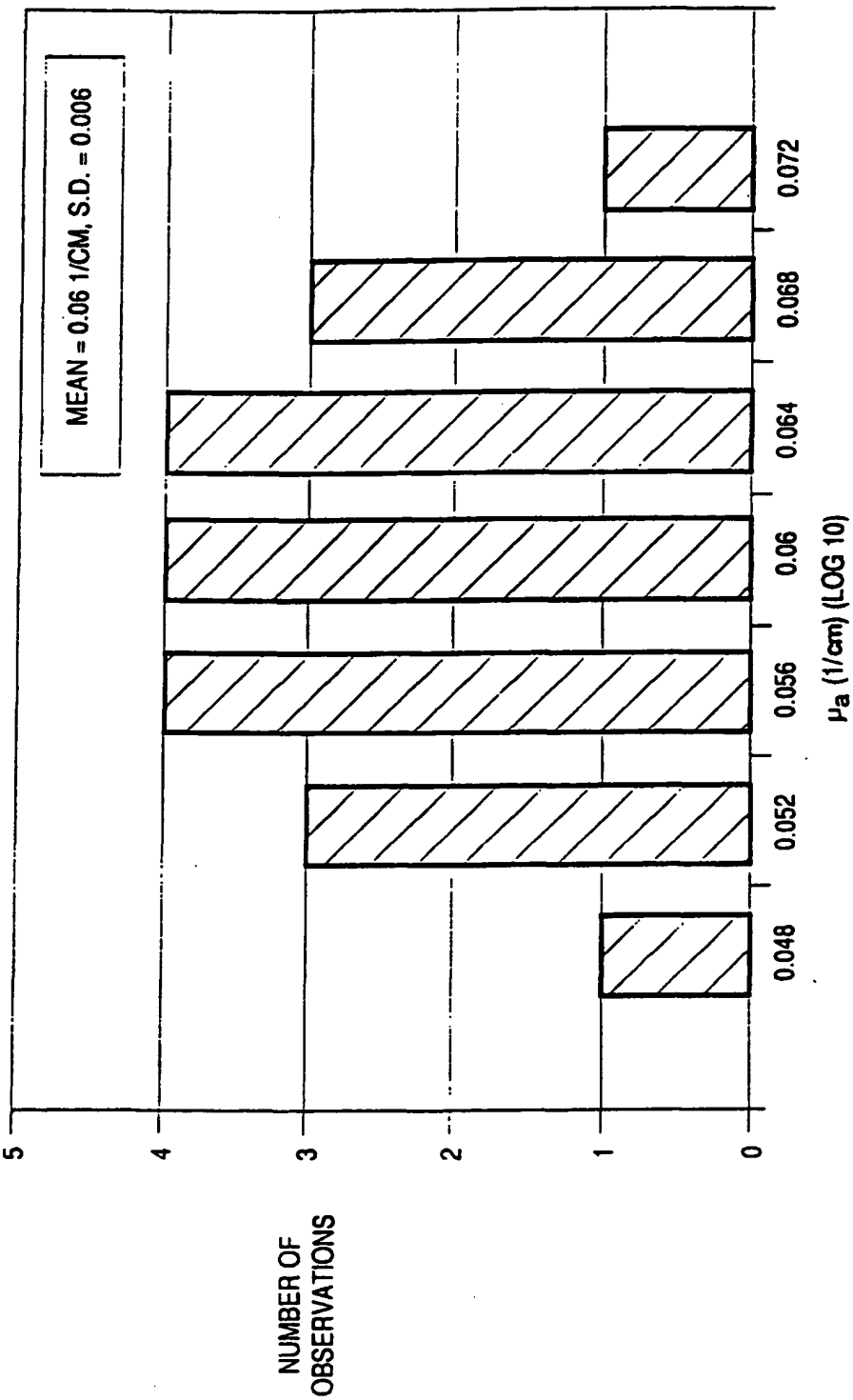
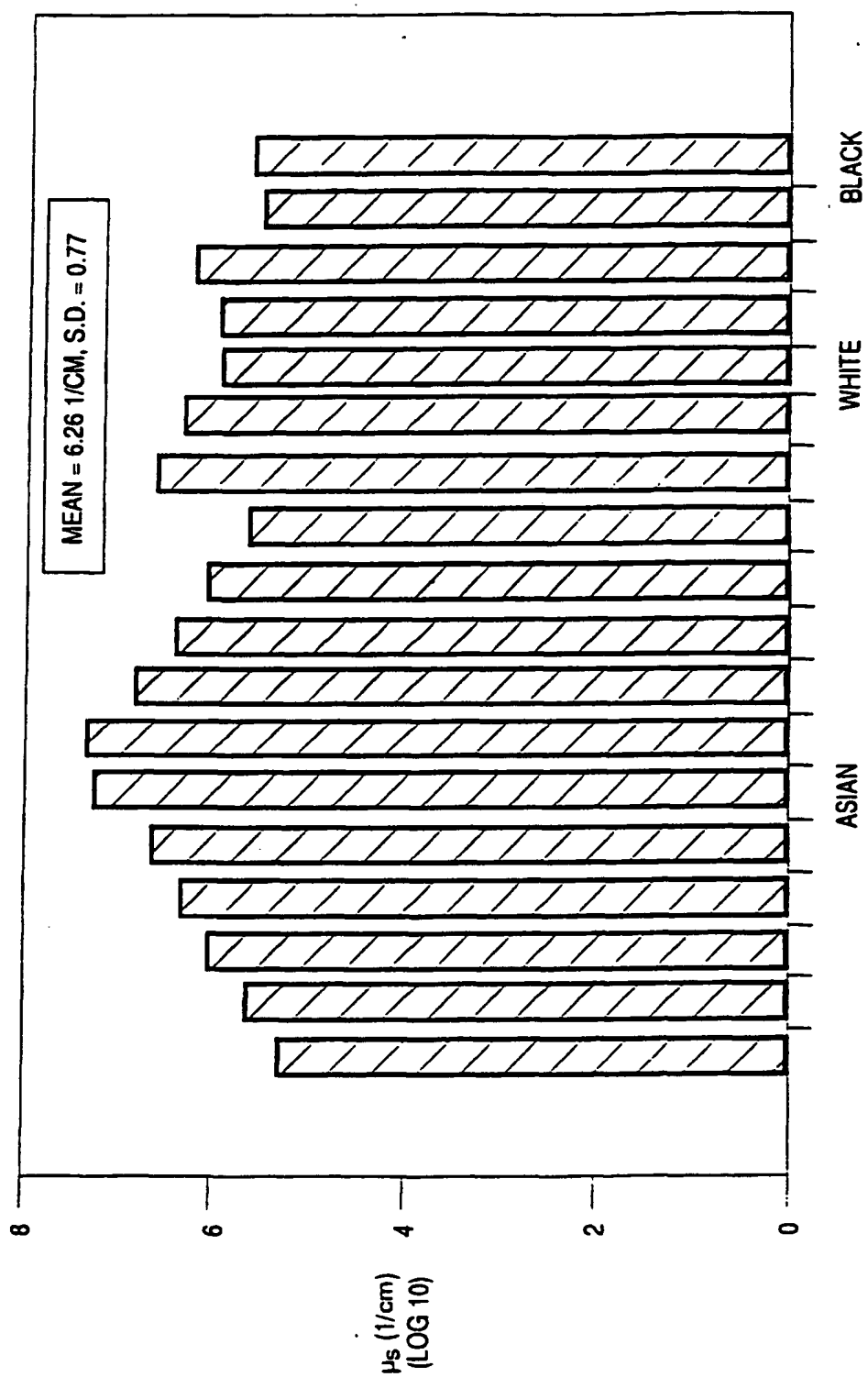

MEAN = 0.06 1/CM, S.D. = 0.006
NUMBER OF OBSERVATIONS
0
1
2
3
4
5
0.048
0.052
0.056
0.06
0.064
0.068
0.072
μ_a (1/cm) (LOG 10)

FIG. 4C

FIG. 4D



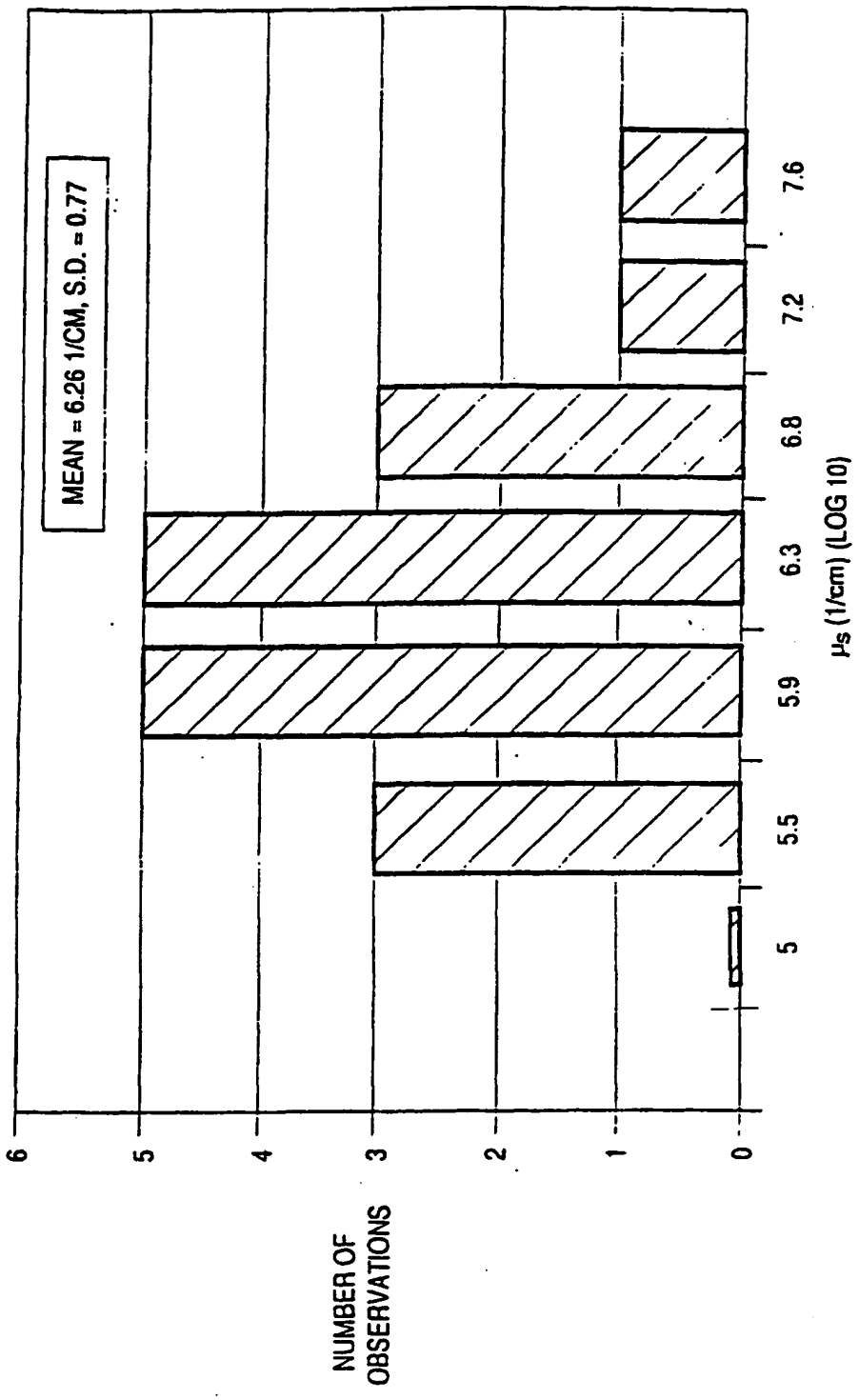

MEAN = 6.26 1/CM, S.D. = 0.77
NUMBER OF OBSERVATIONS
0
1
2
3
4
5
6
5
5.5
5.9
6.3
6.8
7.2
7.6
μs (1/cm) (LOG 10)

FIG. 4E

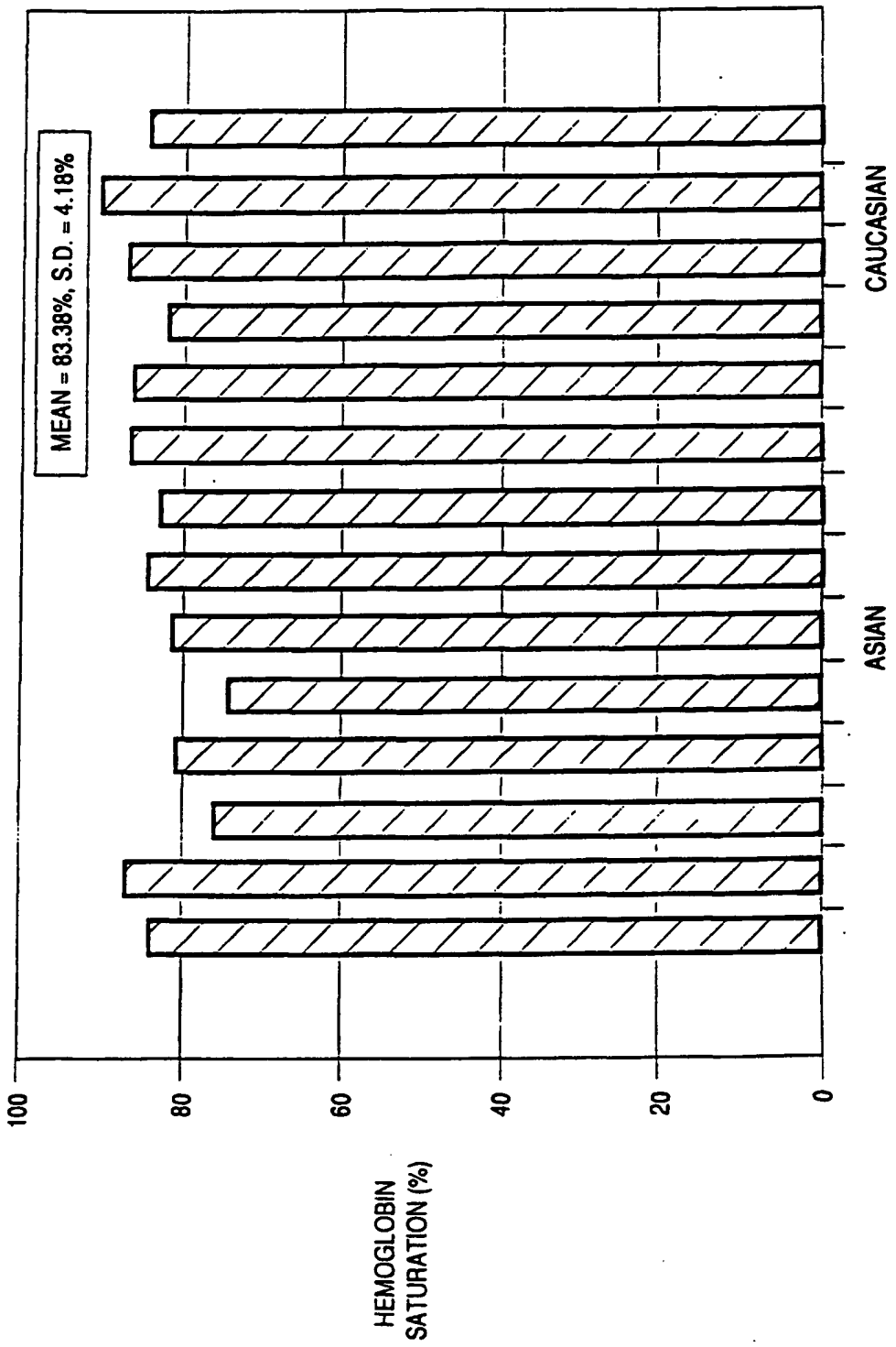

MEAN = 83.38%, S.D. = 4.18%
CAUCASIAN
ASIAN
100
80
60
40
20
0
HEMOGLOBIN SATURATION (%)

FIG. 4F

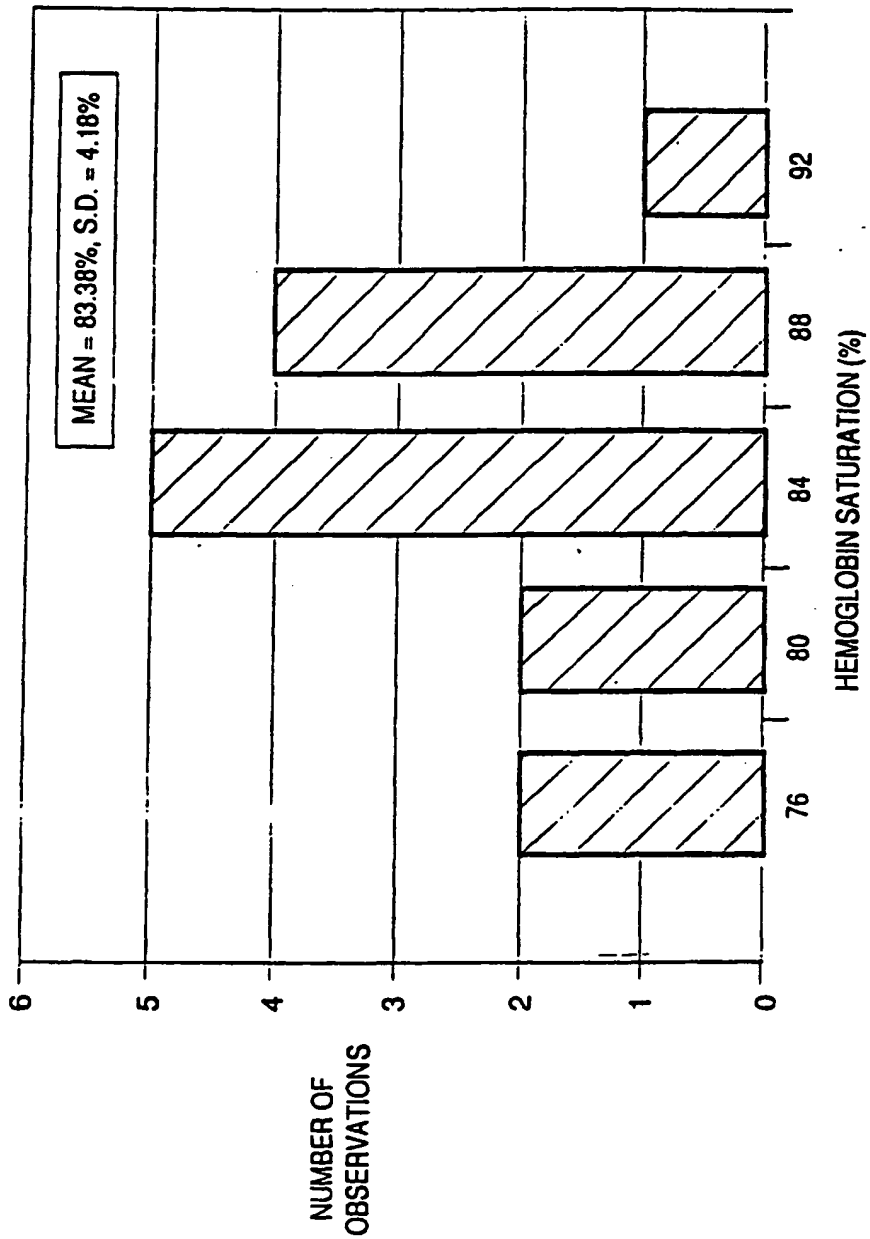

MEAN = 83.38%, S.D. = 4.18%
NUMBER OF OBSERVATIONS
0
1
2
3
4
5
6
76
80
84
88
92
HEMOGLOBIN SATURATION (%)

FIG. 4G